T H E S I S

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on

AN ORIGINAL INVESTIGATION into CUTANEOUS REACTIONS in GONOCOCCAL INFECTIONS.

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I N D E X .

AN ORIGINAL INVESTIGATION INTO CUTANEOUS REACTIONS IN GONOCOCCAL INFECTIONS.

INTRODUCTION.

Recent advances in medical diagnosis have been for the most part in the nature of definite scientific and usually chemical tests, but the observation of effects from the application of certain solutions or substances to the skin has also been noted.

The following is an account of certain work and experiments carried out at East Pilton Hospital and at the Royal Infirmary, both in the wards and in the bacteriological laboratory.

All cutaneous reactions are based on what is known as "The Phenomenon of Arthus". An animal receiving repeated injections of a foreign protein at about six day intervals, shows no reaction at the site of injection after the first three, but/

but after the fourth a local reaction occurs with redness and swelling, and after subsequent injections the reaction becomes progressively more severe and may go on to gangrene.

In gonorrhoea and its complications, whether arising from fresh invasion of adjacent tissues and organs, or those best described as "Metastatic", the most certain method of diagnosis is the discovery of the casual organism, the gonococcus. If the organism can be cultivated and recognised from other members of the Neisseria by special laboratory tests, the diagnosis becomes certain. The demonstration of the gonococcus in properly stained films is the usual method employed.

In recently acquired infections with large numbers of organisms in the discharges, the diagnosis presents no difficulty. However, in cases of Prostatis, Salpingitis, Arthritis, etc., where suspicion is entertained as to the cause, the organism may be present in such small numbers, if at all, that the examination of films gives little help in coming to a definite conclusion. In these cases, cultures present even/

even more remote possibilities, since the large number of secondary organisms which are usually present, minimises the cultural chances of the less numerous and more delicate gonococci.

It has also to be recognised that gonococci, when apparently eliminated from the primary focus of infection, may still persist in the tissues; that, in fact, there may be a systemic infection without local discharge, and that cases of arthritis may develop months or it may be years after the primary infection, when the symptomatic discharge has been in abeyance for some considerable time.

In difficult cases, such as the above, a complement fixation test on the blood serum was investigated as a diagnostic measure, and in the hands of skilled and careful serologists has given good results up to a point. The majority of workers have found the results of this test to be variable, and to some extent unreliable. It is a delicate serological test, requiring much time, skill and care, and has perhaps been more widely used as a means of help in diagnosis, than as a test of cure.

Since/

Since the gonococcus is considered to be a toxic organism and acute infections show definite clinical signs of toxaemia, it is reasonable to assume that a Cutaneous test may be available.

The recent work on detoxicated vaccines gave such investigations greater scope, since the toxic fractions could be obtained separately, and their value if any ascertained.

The following is a list of the substances investigated:-

(1) Detoxicated gonococcal vaccine.

(2) Polyvalent " "

(3) Toxin (Gonococcal)

(4) Lipoid Fraction (Gonococcal)

(5) Proteoses (Gonococcal)

(6) Polyvalent emulsions of gonococci in varying strengths and with varying methods of control.

Previous work on this subject has been done almost entirely by Continental and American workers, and the amount of attention given to diagnostic tests is small as compared with that given to tests of cure.

The/

The Cutaneous test, like the Complement Fixation Test depends on systemic response to infection, but if present has the added advantage of comparative simplicity.

The Experiments throughout were of an entirely tentative nature, and in a great many cases the Complement fixation test was utilised as a control and for purposes of comparison.

IMMUNITY AND SENSITISATION.

A few instances of natural immunity to gonorrhoea have been reported by WELANDER (1,2), EPSTEIN (2) and others. The evidence to the contrary, however, is overwhelming, since numerous experimental inoculations have been reported, and have all been followed by the disease. Moreover, clinical experience is entirely in favour of the absence of any natural resistance in mankind.

Local immunity exists in comparative degree, and probably depends chiefly on histological variation combined/

combined with other accessory factors, e.g. injury or laceration as in the case of the vagina, or overdistension and debilitation as seen in cases of retention of urine.

Focal and general reactions occur after intravenous subcutaneous or intramuscular injections of vaccine, leading to the conclusion that the gonococcus can produce a true bacterial sensitisation. In this connection also the following skin conditions have been noted and directly connected with gonorrhoea, viz:-

(i) Scarletiniform rash.
(ii) Urticarial rash.
(iii) Bullous and haemorrhagic rash.
(iv) Rash resembling Erythema Multiforma.
(v) Rash resembling Erythema Nodosum.
(vi) Keratodermia Blennorrhagica.

These are considered as partly due to circulating gonococci and partly to toxins. In some of the nodular rashes the lesions suppurated and the gonococcus was/

was obtained from them. All the above rashes are what we now understand to be hypersensitive phenomena. HODARA (3), has demomstrated the gonococcus in the blood in these cases, and it is probable that the individual is sensitised to the gonococcus, the rash being the result of the reaction between the sensitised skin, and the organisms brought thereto by the circulation. The cases of Keratodermia Blennorrhagica, published by LEES (4), are described by him as local toxic manifestations. Bacterial sensitisation is said to occur in man, in a way which is analogous to serum sensitisation in guinea pigs injected with horse serum. For 8 to 10 days after the sensitising injections, subsequent injections of the sensitising substance produce no signs of anaphylaxis, but the degree of hypersensitiveness gradually increases from the 10th. to the 21st. day. After this it gradually diminishes, but it never disappears during the whole life of the animal. As an analogy, it is held that persons who have once had a tuberculous infection will give a positive Van Pirquet reaction for the rest of their lives. Among the proteins capable of acting as/

as anaphylactogens are bacterial substances. An animal cannot be sensitised to its own tissues. The only exception to this rule is the lens of the eye.

KOLMER (5) believes that there is no experimental support for the theory that allergic skin reactions may be taken as an index of resistance or immunity. Positive skin reactions do not run parallel with the presence of circulating antibodies. It has been shown (FLEISCHNER & MEYER & SHAW) that guinea pigs showing a high degree of acquired immunity to a organism, as evidenced by strong positive agglutination and complement fixation reactions, and complete resistance to a subsequent infection with living organisms, will never give specific positive cutaneous reactions. A state of anaphylactic hypersensitiveness can exist without the least cutaneous hypersensitiveness. With tuberculin reactions, cutaneous sensitiveness only occurs in the presence of infection.

All evidence goes to show that a positive cutaneous reaction is an indication of sensitiveness and not of immunity.

Before/

Before performing the experiments which are to be described, all the available literature on the subject was searched, and note was taken of previous methods and their results. Practically all the literature is continental, and furthermore was published before the subject of Venereal Diseases was made a separate and special study. In only one or two of the papers is the whole work given to this one investigation, the majority being of a composite nature either in connection with skin diseases or medico-legal work.

KRAUSE (6) did a series of experiments to determine the time which elapses between infection and the appearance of cutaneous hypersensitiveness. This was done for tubercle - those injected with virulent cultures showed increasing hypersensitiveness from the 11th to the 46th day, and in every case it was more intense than in animals inoculated with the non-virulent bacilli. It increased as the disease progressed, but began to heal as the disease came to a standstill, and then during cure became milder, but never entirely disappeared.

STOKES (7) /

STOKES (7) and SELLEI (8) found that normal skin reacts to an intradermal injection of normal skin in the same way as it reacts to an injection of luetin, and STOKES further found that .5 parts Agar in .85 parts saline and 20% Bismuth Sublimate in saline gave reactions similar to luetin. These interesting facts together with later references on the effects on cutaneous tests of taking certain drugs by the mouth, show clearly how all important it is to have proper controls in all cutaneous tests.

DWIETRIEVE (9) states that tests were carried out in 112 cases using 7 different vaccines. Of his cases seventeen had acute gonorrhoea, twenty-six had chronic gonorrhoea, and sixty-one denied gonococcal infection.

The results in every case, contrary to those of FINKELSTEIN and GERSCHUN (10) were negative, and so he concludes that this test is without value. He does not accurately describe his emulsion, but it would appear that it was an ordinary gonococcal emulsion as prepared for a vaccine, used in seven/

seven different strengths. The work is not convincing, since his details about the emulsion are not sufficiently accurate.

FINKELSTEIN & GERSCHUN (10). These authors say that both a Complement Fixation Test, and cutaneous tests after the method of Von PIRQUET are obtainable, and that they are specific for the disease, i.e. are not found in other diseases. They use the upper part of the anterior aspect of the forearm in the cutaneous tests, and apply four tests to each patient.

(1) Gonococcal Vaccine 1,000,000 per c.c.

(2) " " 10,000,000 per c.c.

(3) Streptococcal Vaccine - strength not given.

(4) Saline Control.

THIRTY-EIGHT PATIENTS were treated, and gave uniformily negative results with all four solutions. Ten of the patients suffered from syphilis, ten from soft sore, and eight from tuberculosis; the remainder were healthy and all denied ever having gonorrhoea. Three other patients gave redness without any papule formation/

formation, and in these cases there was some confusion and doubt in regard to history.

In twenty-two patients with acute gonorrhoea (gonococci present in films) seven were positive (i.e. 33%) with the 10,000,000 per c.c. emulsion, and in two of these a positive result was observed with the 1,000,000 per c.c. emulsion. The remaining thirteen showed a negative result (i.e.67%).

In twenty-four cases of chronic gonorrhoea (metastatic lesions) twenty-two reacted as positive (i.e. 92%) with the 10,000,000 per c.c. emulsion, and in twelve of these a reaction also occurred with the 1,000,000 per c.c. emulsion.

The saline control and streptococcal emulsion gave in all cases negative readings. No intradermal injections were used in the above, all the tests being done by scarification as in a Von PIRQUET test.

They conclude that the test is of most value in subacute and chronic forms of the disease, and in 24 cases they had 92% of positives. They do not/

not say whether the emulsion is polyvalent, but its strength is only one fiftieth of the strength which I found to be the optimum. They recommend that more close clinical study and observation is required, and that from other experiments, there is no value in any agglutination reaction.

DECASTRO (11) states that the best method of diagnosis of gonococcal infections by vaccines is the intradermal one, and he goes on to describe in detail a condition of idiopathic hydrocele. The whole article is of a medico-legal nature, and the gonococcal diagnostic tests are merely touched on in passing.

SOMNER (12) states that after 14 days the Complement Fixation Test becomes positive. He concludes from his results that the reaction is specific and of diagnostic value. Further statements are to the effect that a positive is of great value, but a negative does not exclude gonorrhoea as a factor. He worked with Arthigon, a proprietary gonococcal vaccine both undiluted and diluted in carrying out cutaneous tests, and found inconsistent results in both/

both infected and normal individuals, so that he and his co-workers concluded that these tests were of no value.

KOHLER & EISING both consider the intradermal to be more valuable than the scarification methods.

KOHLER (13) used the method of Von PIRQUET with a scarifier, but found it unsatisfactory. After one hour a definite wheal with surrounding redness appeared and then faded rapidly. In normal people the reaction was certainly more fleeting than in others. With Arthigon the wheal was larger, but did not persist for any longer.

The paper by KOHLER, only touches on the subject in dealing with other aspects of gonorrhoea and with treatment, but EISING (14) gives figures, and out of nineteen cases of gonorrhoea, states that sixteen gave a positive skin reaction (i.e. 84%), three gave a doubtful result, but that in all non-gonorrhoeal patients the reaction was negative.

LOUDON (15) found that from eighteen cases, sixteen of the skin reactions were positive, - in three/

three cases of arthritis two were positive. In fourteen normal people, twelve were negative, and in two there was a slight positive result. He also uses the intradermal method, but like the others, does not give accurate details of the emulsion or of his methods.

Different degrees of positivity are described and Arthigon was investigated but pronounced a failure. An ophthalmological reaction was attempted, they do not describe how, but was pronounced as of no practical value.

SATAGUCHI & WATABIKI (16) carried out very full experiments following the Chautamasse method of toxin diagnosis for typhus fever as employed by BRUCH.

They dried up the colonies which resulted from twenty-four hours growth on blood serum agar, and having dried them on a watch glass, extracted them with copper sulphate and distilled water, shook them for forty-eight hours and then heated for one hour at 60° centigrade. The solution was then centrifuged/

centrifuged, and the upper clear layer collected. To this clear fluid they add nine parts of absolute alcohol to one part of the mixture, and the whole is allowed to stand until a deposit appears. This is the alcohol insoluble part. It is dehydrated, and then finally reduced to a grey white powder. A 2% solution is made in distilled water and this is called Gonotoxin solution No.1. They then use a scarification method and rub in the toxin.

They tried this method on twenty patients of whom nine had acute or subacute gonorrhoea, seven had urethritis with prostatitis, three urethritis with epididymitis, and one a condition of sexual neurasthenia. Of these cases only three felt a slight itching at the site of scarification, while two showed a weak reaction after twenty-four hours characterised by slight redness and a minimal amount of swelling. All the others were entirely negative. It was thought that this method would indicate the presence or not of antibodies in the serum, but clinical comparisons made it very doubtful.

A/

A second solution called Gonotoxin No.2 was produced as follows. Cultures were made in horse serum bouillon for three weeks; this fluid culture was heated to reduce its bulk to one tenth of the original volume, and the bulk made up again by the addition of .5% carbolised saline.

A third solution Gonotoxin No. 3. was produced. The growth produced by blood serum agar cultures of 24 to 48 hours duration were mixed with as small an amount of water as possible and heated for one hour at 60° C., and again .5% carbolised saline was added.

The results from the solutions No. 2. and No.3.are not recorded, but are reported as of an indefinite and doubtful nature with the No.2, and of no value of any kind with the No.3.

The accounts given by HODARA & HECHT (17) are of no value in this connection. They are an account of the exanthema said by the authors to be due to circulating toxins, and contain no information about skin reactions.

FUCHS (18) describes experiments made by NEISSER'S/

NEISSER'S method. A nutrient broth is made consisting of -

Bouillon 2 parts.

Ascitic fluid 1 part.

Multiple inoculations of ten or twelve strains were made and the gonococci were then allowed to grow themselves out and die off. The resulting solution resembles Tuberculin in that it contains the remains of the dying and dead organisms, and in addition any toxins resulting from their disintegration. He admits that some slight variation must occur in such different solutions. This solution is either :-

(1) filtered through a Chamberland filter, or

(2) heated at 45°C for one hour, or

(3) kept in the ice chest with .5% carbolised saline as a means of storage.

As a control, an equal amount of the bouillon medium is used. Symmetrical parts of the forearms were used, and the intradermal method was the one employed. In each test the amount injected was .025 c.c.

In all two hundred and eight patients were tested. Clinically these were cases of definite gonorrhoea/

gonorrhoea and the cutaneous reactions were :-

Positive in 161 i.e. 77.4%

Negative in $\frac{47}{208}$ i.e. 22.6%

Further, eighty-one cases other than gonococcal were tested with the following result:-

Positive in 4 i.e. 5.2%

Negative in $\frac{77}{81}$ i.e. 94.8%

He reports that in twenty four hours a definite reaction was present in all those inoculated. In the supposed positives the reaction increased in the second twenty four hours, but in the controls it faded after the first twenty four hours. A difference in the strength of the reaction at the 24 hours interval could often be noted. The results are obtained by rather a complicated process with three "toxins" varying according to length of growth, and he has five degrees in the reading of the reactions. He says that the bouillon control often gave slight reactions but that these never remained more than twenty four hours, and so were negative.

The five degrees of his readings are:-

(1)/

(1) Faint Reaction Fading in 24 Hours.

(2) Reaction Increasing After 24 Hours.

(3) " " " " " with Concomitant symptoms.

(4) " " " " with fever.

(5) " " " " with Lymphangitis and glands in the Axilla. These usually had a feeling of burning and stretching in the skin.

The reactions were all of a transient nature and never protracted or dangerous.

He also used Arthigon and a stock gonococcal vaccine, but he states that the Neisser vaccine was much better. Later in the article he states that the degree of positivity depends on the degree of involvement of the genito-urinary tract and its adnexa. The early prostate cases are either negative or very strongly positive, but the spread of the disease to the epididymis has no effect on the positivity. Some cases, negative in the early stages, become positive later. Treatment by vaccines seems to have little or no effect, and certainly does not cause/

cause a skin reaction to be more marked. When sufficient time elapses after cure, the test cannot be elicited. It is of no importance in determining the cure, and should only be considered when an earlier positive now becomes negative. It never becomes negative while there is still anything of the infection alive. Thus, he claims, one can determine the difference between a true metastatic gonorrhoeal lesion, and some other condition simply following on gonorrhoea.

BRANDWEIMER & HOCH (19) have two articles, the first dealing with Arthigon, where after many attempts and various dilutions, they gave up without coming to a definite conclusion. They then deal with monovalent, polyvalent and autogenous emulsions, and find the latter giving a good reaction, the monovalent giving no reaction, and the polyvalent very unreliable results. It is not a very informative paper.

HEYNEMAN (20) goes on very much the same lines as the above with Arthigon and other vaccines, his cases being chiefly Salpingitis, but concludes that Cutaneous tests are of no value.

C./

C. BRUCH (21) claims to be able to produce a cutaneous reaction in gonorrhoea similar and analogous to the Von PIRQUET in Tuberculosis, and to the Trychophytin test in Tinea. He gives no indications as to how he made his solution or as to his technique. He did tests on thirty patients. Of these thirteen had existing or healed gonorrhoea and of the thirteen eleven were positive, one doubtful, and one negative. Of other seven, two were positive, and these had had gonorrhoea 4 and 18 years previously. The remaining five were negative, although they had had gonorrhoea 6, 12, 15, 18 and 20 years prior to the test. Of ten people who had never had the disease, eight were negative, and in two the result was uncertain.

WOLLSTEIN (22) found that intraperitoneal injections of fresh living gonococci were virulent to guinea pigs and mice. After subculture to seventeen or eighteen generations this virulence decreased by one half. She also found that when the gonococcus is cultivated on certain media, autolysis of the organism occurs even in 24 hours. This tendency to autolyse varies/

varies with the nature and mode of preparation of the medium, and in THOMSON'S (23) medium it is almost eliminated. It was found by WOLLSTEIN that the gonococcus autolytic enzyme was killed by heating at 65°C., for thirty minutes. THOMSON'S experiments however, prove that autolysis depends almost entirely on the alkalinity or otherwise of the suspension. The gonococcus is very soluble even in dilute alkalies, and a suspension of .5% carbolised saline kept in the ice chest will not autolyse for many months. Since the toxin is admittedly an endotoxin and not an exotoxin, it is only liberated by the occurence of autolysis in the suspension.

The gonococcus grows in broth only with difficulty, and if it does so, immediately produces involution forms and dies out. It becomes therefore, impossible to get filtrates from broth cultures which would be more useful than emulsions from other growths.

It was found by TORREY (24) in 1907, that if an emulsion of gonococci in normal saline was shaken for a number of hours, and then filtered, the resulting filtrate was decidedly toxic to guinea pigs. Since/

Since it was almost universally agreed that the gonococcus does not produce an exotoxin, the toxic effect of the filtrate obtained by TORREY must be ascribed to endotoxin liberated into the saline during the process of shaking. Autolysis and disintegration of the gonococci would be necessary for the liberation of any endotoxin.

McCLINTOCK & CLARK (25) have also carried out experiments on the phenomenon of autolysis. They noted that when gonococci were suspended in normal saline for twelve to twenty four hours at room temperature, they lost their affinity for methylene blue; moreover the emulsion began to lose in density and the amount of deposit became gradually greater. A freshly prepared emulsion of the organisms took up the methylene blue stain readily, and they considered that the loss of staining power was due to autolysis. According to this view, therefore, autolysis occurs rapidly in saline suspensions at room temperature. It, however, the suspensions were heated, the autolysis was delayed or entirely inhibited. The addition of 4% tricresol appeared further to defer the autolytic/

autolytic process. They concluded that permanent staining i.e. complete inhibition of autolysis was secured by heating the original saline suspension to 60°C for one hour in the presence of 4% tricresol or by heating th 70°C for one hour in the absence of tricresol.

There are thus numerous theories regarding autolysis, but THOMSON'S experiments are the latest and probably most correct. In spite of his theory that in the ice chest and with .5% carbolised saline added they should not autolyse for many months, it was found that deterioration for cutaneous test work had set in in about one month, and that in three months time the emulsion had become quite unreliable. The same patients are usually in a very different clinical condition in three months time, and so the identical tests could not be repeated, but similar ones showed a marked deterioration in the general sharpness and appearance of the tests, and many more negatives were produced.

DESCRIPTION/

DESCRIPTION OF EXPERIMENTS.

Begun in 1923 at East Pilton Hospital, the work was continued chiefly at the Royal Infirmary, until 1925. The total number of patients on whom tests were made was 571, and the total number of actual intradermal injections about 1200.

Supplies of Gonococcal Toxin, Lipoid Fraction, and Proteoses were obtained from the Pickett Thomson Research Laboratory, London, and were replaced as found necessary to complete the experiments and tables given later.

In gonococcal emulsions there are acid soluble, alkali soluble, and ether and alcohol soluble toxic fractions.

1. The gonococcus is dissolved in alkali, acid is then added and the metaprotein is precipitated. This is the bulk of the detoxicated vaccine.
2. The acid supernatant fluid contains the proteosis, and these are thrown down either by/

by alcohol or a saturated solution of ammonium sulphate.

3. The supernatant alcohol above the proteose precipitate contains a toxic substance which is left when the alcohol is evaporated. It is a brown sticky substance soluble in water. This is the toxin solution (not standardised).

4. When the gonococcus is treated with alkali 98% of it dissolves, but a small portion of it does not dissolve in alkali. This is swung out of the turbid solution by a centrifuge, and the residue is found largely to dissolve in alcohol. The part which dissolves in alcohol is the lipoid fraction. This is insoluble in NaOH. The proteose is standardised to 100,000,000 organisms per c. c. The toxin and lipoid fraction form their nature, and their difficulty in solubility cannot be accurately standardised.

TECHNIQUE/

TECHNIQUE EMPLOYED.

For all tests, the flexor aspect of the forearm just distal to the elbow was the part employed. This ensures accessibility, freedom from hair, and known sensitiveness. The control was always placed nearer the elbow the sensitiveness being greatest at that site.

The method employed was the intradermal injection of the desired quantity of the substance to be tested. A graduated 1 c.c. syringe and a fine (No. 27) needle were used. The skin was first cleansed with soap and water and ether, but not so vigorously as to cause an erythema of the part to be employed. The actual technique, in short, is exactly the same as that used in the Schick test. Other methods are :-

(i) Scarification. This was tried, a "Scarifier" with 9 small points being used, but the results were less satisfactory, the readings being less "sharp", and with a similarity, which made differentiation difficult.

(ii)/

(ii) Rubbing the suspected antigen in and allowing it to dry.

(iii) Rubbing in an ointment and suspected antigen being absorbed with the ointment basis.

These last two tests which depend on rubbing and drying, and absorption from an ointment basis did not seem to have a place in this type of work, and consequently were not employed.

For a diagnostic test, the most attractive method is the intradermal. The question at issue is the measure of the patient's susceptibility, and the intradermal is the only means whereby an accurate given quantity of any solution can be injected.

In asthma, hay fever, prurigo and urticaria, CHANDLER and WALKER and ATKINSON report that the intradermic test is much less specific than the Cutaneous one. It is too sensitive, more difficult to carry out, may cause the patient considerable discomfort, and does not separate closely related proteins, and so they prefer the ordinary cutaneous tests. The bacterial antigen, however, seems to respond differently to the food proteins. In dealing with the protein/

protein sensitiveness, it is recognised that symptoms of definitely bacterial origin and those of other protein origin, must be investigated differently. The usual parenteral proteins give good cutaneous tests, but when bacterial proteins are responsible for symptoms, it is recognised that they cannot be investigated in the same way, since hypersensitiveness, if it appears in cutaneous tests, will then probably be a secondary complicating factor. There is the marked discrepancy in the time taken for the reaction to appear, and in the work done with the gonococcus, the intradermal test was certainly more satisfactory than the ordinary cutaneous one.

The histo-pathology would seem to have some relationship to the time taken for the lesion to appear and mature, and further, although less directly, to the best method to be employed for its production.

STRICKLER, and STRICKLER & ASNIS (26) examined the skin microscopically in Von PIRQUET and leutin tests. In the former they observed a mononuclear cellular infiltration, and in the latter a deep polymorphonuclear infiltration with congestion and/

and necrosis. Typical giant cell nodules have been found at the site of old tuberculin injections. The ideal intra-cutaneous test has only transient cellular infiltration, with, it may be, minute haemorrhages owing to the needle having penetrated just too deeply. The chief difficulty in carrying out the test is to inject into the same depth of skin each time, but with care and practice this is attainable in 90% of cases.

The ideal result of a good intra-cutaneous test is a very definite red erythematous areola, irregularly oval or circinate with fading margin, and with or without a small central wheal. It must be at least twice the size of any control

Time taken for test to appear, and reading of the test

The more intense the reaction the more quickly will it appear. The very striking reactions with large irregular wheals, described later as obtained from the use of autogenous emulsions on patients with complications, appeared in 10 to 15 minutes./

minutes. The erythema which seemed to be the optimum test appeared in 6 to 18 hours, and persisted for from 36 to 48 hours. Altogether 24 hours interval was found to be the best time at which to make readings. Test solutions were found to differ with regard to the exact nature of the lesion produced e.g. the lipoid fraction tended very much to cause papule formation, whereas the toxin, especially when concentrated, tended to produce a rather flat petechial area. The emulsions of organisms tended to produce wheals, if a strong positive was recorded. The ideal positive was considered to be a red areola with or without an irregular wheal, but with an area of erythema spreading in all directions. It was not necessary to have both wheal and erythema present before a positive was recorded.

The test erythema in all cases must be at least twice the size of the control before being considered positive.

GONOCOCCAL TOXIN.

Tests were carried out on 210 different patients with toxin solutions of varying concentration.

Firstly .1 c.c. of pure gonococcal toxin was injected intradermally on seven patients at East Pilton Hospital. Of these seven, four were females in whom gonococci had been found recently in the urethra or cervix, the remaining three were congenital syphilitics. All showed a marked red areola in fifteen minutes, but without any sign of wheal formation. The reaction was most marked in two of the four patients who had gonococci present, and they complained of a stinging pain for some hours. Thus it would appear that they were more susceptible than the others. One girl who had had pyelitis, salpingitis and an arthritis of undoubted gonococcal origin, gave the most intense reaction of all, the areola in her case covering the whole of the front of the elbow, and a good part of the forearm.

Dilutions/

Dilutions were then made, and further tests proceeded with until a dilution was found where discrimination between positives and negatives might be made. With pure toxin or concentrated dilutions the intense local reaction was very general in both gonorrhoeal and other patients, but this was in marked contrast to the entire absence of any constitutional upset even of the slightest nature.

Further tests were carried out with progressively greater dilutions, and the intensity of the reaction gradually diminished. It quickly became evident that a very small amount of actual toxin would be required for the purpose of causing definite negative reactions to which others could be comparable. After repeated trial by experiment, it was decided that .000001 c.c. would be given an exhaustive trial. The same dilution heated at 80°C., for 10 minutes to destroy the specific toxin was used as a control. The clinical notes, the bacteriological findings, the gonococcal Complement Fixation Test and the WASSERMANN reaction were used as further sources of/

of information from which tables were constructed in each case. The tables are given in their various places.

From the TOXIN TABLES the following are the percentage results, when compared with the clinical, bacteriological and other findings.

TOXIN.	Amount injected .1 c.c.	
TEN CASES	(50% correct (30% false negatives (20% false positives	Vide TABLE No I page 60
	Amount injected .01 c.c.	
TEN CASES	(70% correct (30% false negatives (0% false positives	Vide TABLE No I page 60
	Amount injected .001 c.c.	
SIXTEEN CASES	(75% correct (25% false negatives (0% false positives	Vide TABLE No II page60-62
	Amount injected .0001 c.c.	
THIRTY NINE CASES	(56% correct (40% false negatives (4% false positives	Vide TABLE NoIII page 63-4
	Amount injected .000001 c.c.	
EIGHTY THREE CASES	(72% correct (25% false negatives (30% false positives	Vide TABLE No IV page66-72

In deciding as to the correctness of any test, clinical signs and bacteriological findings were stressed, and unless the cutaneous reaction agreed with them, the case was grouped in either false negatives or false positives. In considering the cutaneous reactions which did not agree with the Complement Fixation Test and the history of the patient we erred on the side of giving more weight to the Complement Fixation Test and the history than to the cutaneous test. It appeared that this was the only possible way to construct tables with a view to precluding the possibility of the results appearing better than they should be.

The Tables and the deductions made from them are thus as accurate as possible, and cannot be considered inflated.

For example, in a neurasthenic patient with no symptoms of Venereal Disease of any kind, if the Complement Fixation Test gave a positive reaction, it was considered that the cutaneous test should give a positive also. If, again, the Complement Fixation Test gave/

gave a negative result after a course of vaccines, a negative cutaneous reaction was considered essential to be correct.

It was incidentally noted in the research that this cutaneous test had some prognostic value, although difficult to prove by facts and figures. Many of the false negatives in the tables are met with in cases suffering from complications of gonorrhoea. These cases with a marked clinical condition, although no reaction occurs at the site of the injection of the toxin, usually make very good and very rapid recoveries. They apparently had sufficient circulating auti-toxin in their tissues to neutralise the small amount of toxin injected. This is analogous to the SCHICK Test Theory, but on following it up, it was found that the prognostic value was not sufficiently reliable to justify further trial along these lines.

DETOXICATED/

DETOXICATED VACCINE.

The vaccine as supplied for therapeutic purposes by the Pickett-Thomson Research Laboratory, London, was the one experimented with, 0.1 c.c. containing 2,500 millions gonococci.

Firstly 0.1 c.c., and then dilutions up to .0001 c.c. were used. All the tests tended to show a small red erythema after the white raised area at the point of the injection had disappeared, and the intensity of it and the time for which it persisted depended more on the concentration of the solution than on the condition of the patient. In no case was a wheal produced. It was found that 0.1 c.c. of the ordinary detoxicated vaccine was better than any dilutions, but there was obviously too much difficulty in striking a medium between the risk of a moderate number of false positives with a strong solution, and a very large number of false negatives with a weak solution.

From the table of 12 cases the result is as follows./

follows. The negatives were supplied by those with no infection or with an overwhelming infection e.g. a prostatic abscess. A dose which would discriminate between a doubtful positive case and a negative case, and yet remain consistently negative with known negatives was difficult to estimate.

0.1 c.c., containing 2,500 millions gonococci.

TWELVE CASES	(52% correct (32% false negatives (16% false positives	Vide TABLE No V page 73

LIPOID/

LIPOID FRACTION.

As already noted, this is the alcohol soluble part of the alkali insoluble part of the gonococcus. For no apparent reason either by its nature or its appearance, this proved perhaps the least reliable or suitable of all the solutions tried. There was a distinct and constant tendency for the formation site of a papule at the site of injection.

In the dilutions considered suitable for a test, this papule appeared in twelve to eighteen hours and remained for one, two, or even several days.

After proceeding on the same lines as with the toxin, i.e. using diminishing amounts thus, 0.1, .01, .001, .0001, etc., of a c.c. it was found that the papule formation did not cease until at each injection there was used a dilution representing .000001 c.c. lipoid fraction at each injection.

At this dilution and with the same clinical, bacteriological, and serological findings as controls, the results of the table are as follows:-

	.00001 c.c. lipoid fraction	
THIRTEEN CASES	(46% correct (46% false negatives (8% false positives	Vide TABLE No VI page 74

GONOCOCCAL PROTEOSES.

These are obtained from the acid soluble portion of the gonococcal emulsion by precipitation either with alcohol or with a saturated solution of ammonium sulphate, and the solution is standardised to contain 100,000 million organisms per c.c.

The Proteoses solution was much more amenable and satisfactory for cutaneous tests than either the Lipoid or the Detoxicated Vaccine. The same method of investigation by steadily diminishing doses was followed, but in addition other forms of test with this substance, such as boiling it, and other controls were attempted, as will be seen in the tables.

Commencing with 0.1 c.c. various dilutions were used up to .0000001 c.c. and then controls of the same dilution but boiled for 5. 10 or 20 minutes. The details are shown in the tables, and the results of these are as follows:-

.001 and .0001 c.c. Proteoses.

TWENTY TWO CASES	(69% correct (20% false negatives (11% false positives.	Vide TABLE NoVII page 75-6

.00001 c.c. Proteoses

TWENTY FOUR CASES	(50% correct (29% false negatives (21% false positives	Vide TABLE NoVIII page 77-9

.0000001 and .000001 c.c. Proteoses

NINETY EIGHT CASES	(70% correct (16% false negatives (14% false positives	Vide TABLE No IX page 80-8

.0005 c.c. Proteoses and boiled Control

FORTY FOUR CASES	(68% correct (23% false negatives (9% false positives	Vide TABLE No X page 89-91

POLYVALENT/

POLYVALENT GONOCOCCAL EMULSION.

Pure cultures of gonococci were obtained from the urethral discharge of fresh untreated cases as they reported at the V.D. Department Ward V.A., the Royal Infirmary. Slope culture tubes on THOMSON'S medium or on laked blood agar enriched with glucose were inoculated and immediately transferred to a bacteriological incubator in the department. The water of condensation and uniform consistence of the media were preserved by having the tops of the test-tubes covered with firm rubber caps. Within a few seconds the loopful from the suspected discharge was transferred to the incubator slope, and thus pure cultures were usually obtained. Occasional contaminations necessitated subcultures, but all second and further subcultures were made as heavy as possible so that sufficient growth might be obtained for emulsification, and the need for subcultures reduced to a minimum. Thus any changes in the organism as a result of repeated subculturing were avoided.

The/

The organisms were cultivated for 48 hours, at 37°C., and the growth was then removed by sterile platinum loop and emulsified in .5% carbolised saline. The emulsions were stored in the ice chest, the cotton wool stoppers being covered by a fixed rubber cap. These were then utilised as chosen for the production of polyvalent emulsions, desired quantities being removed by sterile pipette and mixed in a fresh sterile test tube.

To obviate contamination all cultures were examined microscopically before emulsification; diphtheroid bacilli were found to be the most frequent cause of contamination.

The polyvalent emulsions were stored in amber vaccine bottles with rubber cap, the required quantities being removed by syringe as necessary.

Regarding "polyvalency" and "strains", the growths obtained from any one patient, and emulsions made therefrom were considered one "strain" of gonococcus.

Since there are said to be about seventeen strains from the bacteriological standpoint, it became/

became very difficult to get anything which could be called "polyvalent" and also fresh. The uncertainty of a constant supply of new cases, and the difficulty at times with contaminations made this work a difficult practical problem.

Firstly, various "polyvalent" emulsions of strengths varying from 5 to 50 million gonococci per c.c. were tried on known negatives among the staff in the laboratory. These emulsions gave fairly uniform results,-a little more definite with the stronger emulsion - and consisted of a small mild red erythema which appeared in 6 to 18 hours and faded in about 48 hours.

Two polyvalent emulsions were employed in the experiments. The first contained eight and the second twenty "strains".

With the first, the total quantity was utilised in tests with varying strengths in order to find out what strength gave a good positive and a definite negative when properly controlled.

It was found by repeated experiment that the optimum/

optimum strength was 537 million gonococci per c.c., as estimated by the barium sulphate opacity scale method, and the control consisted of the same emulsion heated for one hour at 80°C.

With the second emulsion the same strength and controls were utilised but the presence of twenty "strains" made it more polyvalent.

TEST. 0.1 cc. of emulsion containing 537 million gonococci per c.c.

CONTROL. 0.1 cc. of emulsion containing 537 million gonococci per c.c. heated for 1 hour at 80°C.

SIXTEEN CASES	(81% correct (6% false negatives (3% false positives	Vide TABLE No XI page 92

As can be seen at once, these results are much better than those obtained from the previous experiments with any other preparation.

From the list of strains given after tables a record of each patient from whom cultures of gonococci were obtained, was available, and thus during the/

the preparation of the polyvalent emulsion experiments could be carried out with regard to apparent virulence, and with regard to sensitiveness to monovalent or polyvalent emulsions.

PATIENT A. Seen at outpatient department with severe anterior urethritis. Culture from urethral discharge yielded profuse pure Culture of Gonococci. This was emulsified in the usual way and stored for use as a gonococcal emulsion. Eighteen days after first reporting, this patient developed a severe posterior urethritis, with acute prostatitis short of abscess formation. He had a temperature reaction, was pale and felt ill, and gonococci were still numerous in the discharges.

Employing the same technique as before the following cutaneous tests were carried out on the patient's forearem.

Intradermal administration of -

(1) Polyvalent Emulsion - Eight recent strains not containing the patient's gonococcus.

(2) Polyvalent Emulsion - Same as above, but containing patient's gonococcus.

(3) Monovalent Emulsion - Patient's own gonococcus.

In/

In each case .1 c.c. was injected and each emulsion was at 537 millions gonococci per c.c. as estimated by opacity scale. The results were:-

(i) Negative

(ii) Weak positive. Erythema.

(iii) Large distinct surrounding area of redness developing immediately after the injection. In fifteen minutes a definite wheal had formed with surrounding pseudopodeal areas of erythema. The patient complained of intense burning and itching, which has completely passed off in 1½ to 2 hours.

In two other patients reporting in the same way and who later developed complications with pyrexia and apparent toxaemia, similar experiments gave exactly the same results.

In a larger number who did not suffer from apparent toxaemia and pyrexia, almost exactly one half gave frankly negative results to the polyvalent emulsion which did not contain their own organism, while the emulsion containing their own gonococcus always gave a definite positive result. The polyvalent emulsions used all contained from five to ten "strains".

A/

A better control might have been afforded by the use of a polyvalent emulsion containing from seventeen to twenty strains. The difficulty in this respect was with regard to the deterioration which is apt to occur when emulsions are kept. Even under apparently ideal conditions the supply of fresh pure cultures was sometimes uncertain. It was considered better to use five to ten recent fresh and certainly active strains than more numerous, less uniform, and some of them less active ones because of deterioration as a result of age.

The results of the above experiments would appear to prove that there are strains of gonococci and that freshness and polyvalency are absolutely essential for good results.

As with animal and vegetable proteins, so with bacterial proteins, group reactions may occur, although some observers maintain that bacterial anaphylaxis is absolutely specific for each organism. In this connection KARSNER AND ACKER (27) quote GAY AND MINAKER'S work on the intra-cutaneous reaction for/

for the detection of meningococcus carriers. The meningococcus is a member of that group of gram negative diplococci named the Neisseria and is morphologically indistinguishable from the gonococcus. In the laboratory they are differentiated by their fermentative powers on sugars. These workers use an emulsion of powdered meningococci of five strains and obtain reactions in 64.5% of known carriers, and in 26.4% of non-carriers.

They do not consider it useful in diagnosis, but suggest that in carriers there is some degree of acquired resistance.

It is of further interest in this connection that, whereas it is now accepted that the presence of a specific cutaneous reaction to any given substance is a sign of hypersensitiveness to that substance, the degree of reaction in Enteric fever with "typhoidin" has been interpreted as an indication of the degree of immunity. It has been said to be due, in rabbits, to sensitisation to the bacterial proteins, and that it is not an antigen-antibody reaction. Most other workers/

workers accept the theory of protein sensitisation and that the reaction is no index of immunity.

Pneumonia, hydatid, disease, whooping cough, soft sore, tinea, and leprosy had further been investigated for cutaneous test, but in all cases with failure from any useful diagnostic point of view.

VAUGHAN AND WHEELER (29) think that when a protein antigen is injected, the tissues produce a specific ferment which digests it and splits up the protein. By boiling up the proteins with an alcoholic solution of sodium hydrate, they split up the protein into a non-toxic alcohol soluble part, and a toxic alcohol insoluble part. The toxic part, when injected into normal guinea pigs, causes death with all the symptoms of anaphylactic shock. This toxic part can be obtained from all proteins and seems identical in all. The specificity of the reactions is due to the non-toxic part of the protein, which varies in each case. Work has also been done on Cutaneous susceptibility to drugs, and on the effects of drugs on other specific Cutaneous tests. The effect of Potassium/

Potassium Iodide on the luetin reaction is well known. SMITH (30) found that guinea pigs and rabbits sensitised to ox or horse serum, if treated with moderate doses of quinine previous to the injection of the specific antigen, had their susceptibility increased from 3 to 10 times as compared with control sensitised animals. The conclusions otherwise are that no skin test is reliable as a guide to which drug, if any, is causing a rash. Nor is it of any value in determining what drug, if any, can be given to a patient with safety.

These last paragraphs although of indirect interest, are briefly touched on to enable the subject to be as complete as possible.

Thirty grains of quinine were given to a few in-patients simultaneous to the injection of the polyvalent emulsion and no apparent difference was seen. One could not have standardised controls as with guinea pigs as in the tests of SMITH but known negatives and positives in the same clinical condition were used. Alcohol, however, was definitely observed to influence the test and when being freely indulged in, the tests became much more positive.

CONCLUSIONS.

As can be readily ascertained, the most successful results were from the polyvalent gonococcal emulsion. The others presented great variations, and certain dilutions of toxin and proteose were also useful.

The results of these three substances are comparable to, if not better than the results of the Complement Fixation Test, but the difficulty with the emulsion is the constant supply of a fresh and polyvalent preparation containing "good strains", and therefore able to detect the maximum number of correct positives.

Could that supply be ensured, the ease of application and the quick reading of the test either in hospital or in private practice would make it a helpful adjunct in cases of difficult diagnosis.

1./

1. Various gonococcal cutaneous tests are available in the following order of merit.

(a) Fresh Polyvalent Gonococcal Emulsions.

TEST - 0.1 cc. of emulsion containing 537 million organisms per c.c.

CONTROL - 0.1 cc. of emulsion containing 537 million organisms per c.c. heated at 80° C for 1 hour.

Amount use - 0.1 c.c.

Correct readings 81%
False Negatives 6%
False Positives 3%

(b) Gonococcal Toxin.

TEST - .001 cc.

CONTROL - .001 cc. heated at 80°C for 10 minutes.

Correct readings 75%
False Negatives 25%
False Positives. 0%

(c) Gonococcal Proteoses.

TEST - .000001 cc.

CONTROL - .5% carbolised saline.

Correct readings 70%
False Negatives 16%
False Positives 4%

(d) Detoxicated Vaccine.

TEST - .1 cc. Vaccine containing 25,000 millions gonococci per. c.c.

CONTROL - .5% carbolised saline.

Correct readings	52%
False Negatives	32%
False Positives	16%

(e) Lipoid Fraction.

TEST - .00001 cc.

CONTROL - .5% Carbolised Saline.

Correct readings	46%
False Negatives	46%
False Positives	8%

2. The intradermal method is more suitable and more accurate than scarification methods.

3. The gonococcal cutaneous reactions are not influenced by the taking of drugs or the administration of vaccines. Indulgence in immoderate quantities of alcohol tends/

tends markedly to produce false positives

4. From a diagnostic and therapeutic as well as a bacteriological standpoint there appear to be "strains" of gonococci.

5. Emulsions intended for use in this test must be both fresh and polyvalent; these terms having the significance conveyed by their explanations in the previous pages.

6. The more remote the history, and the less definite the clinical findings, the less helpful and less definite becomes the test.

7. A definite positive skin reaction obtained with a fresh polyvalent emulsion is strong evidence of gonococcal infection.

8./

8. A negative skin reaction obtained in a suspicious case does not preclude the diagnosis of gonococcal infection.

I would like to take this opportunity to express my thanks to Dr. W.R. Logan, bacteriologist, to the Royal Infirmary, Edinburgh, to my associates both in the laboratory and in Ward VA, and to all the members of the staff both in the laboratory and Ward for their constant and unfailing help. My very grateful thanks are due to Dr. David Thomson, London, for his generous supply of toxin, lipoid fraction, and proteose, and for his permission to publish the results. Finally, I can scarcely express in words my indebtedness to Mr. Lees, without whose constant stimulation, help, and kindness the work could never have been carried through.

I also hereby declare that this work has been carried out entirely by myself while working either in the wards or in the laboratory at the Royal Infirmary.

George Brewer

"STRAINS" of GONOCOCCI used in various EMULSIONS.

REFERENCE NUMBERS of PATIENTS.

A 143

A 1458

3836

A 1706

A 1602

A 1663

A 1635

3847

3845

A 1762

A 1586

A 685

A 1748

Case of salpingitis from Ward 36.

Dr. L's case of vulvovaginitis in girl age 9.

A 1828

A 1858

A 2074

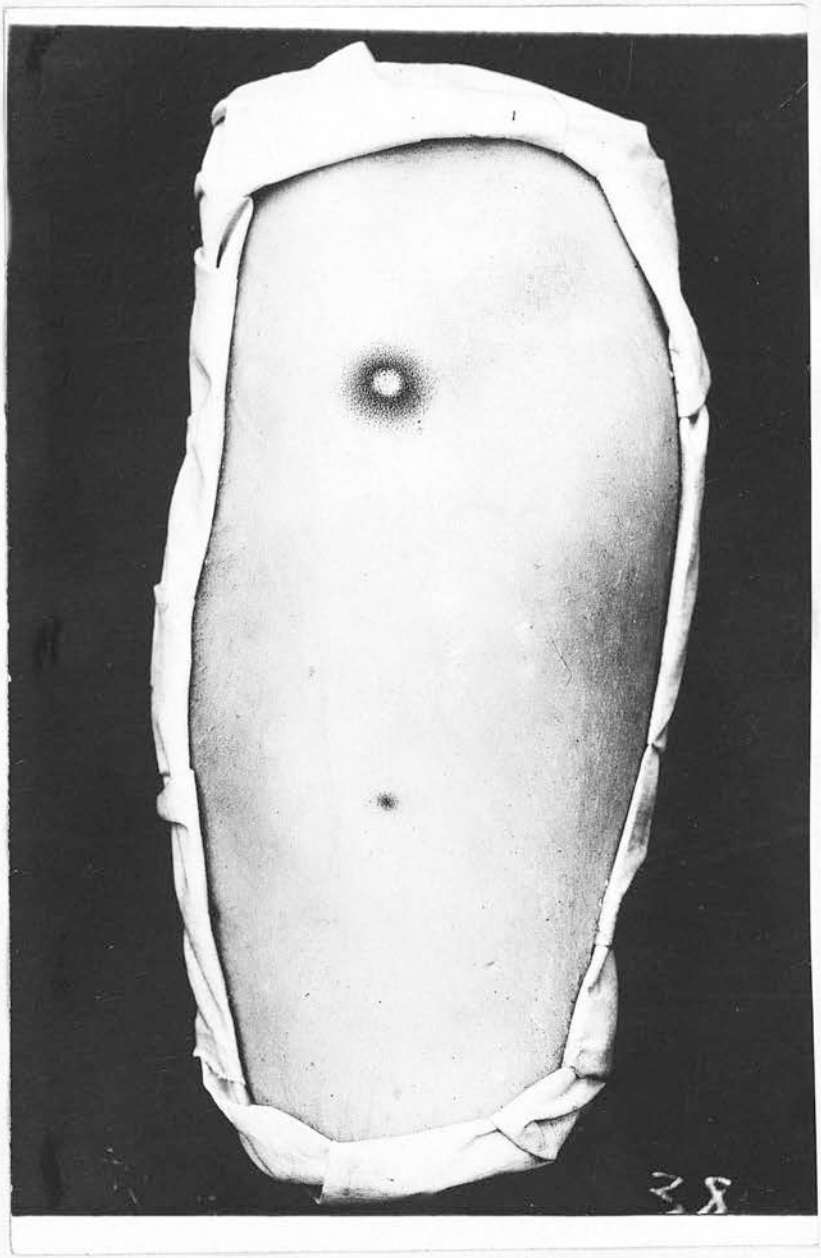
A 2118

Four strains from Ward VA - numbers unknown.

The following numbers provided the cases on whom the tests were carried out in order to prove the sensitiveness of a patient to his own gonococcus, and to show how essential it is that emulsions should be polyvalent.

A 2263)
A 2311) These therefore come from
A 2173) clinically virulent cases.
A 2318)
A 1405)

The final strength of emulsion used in the tests was 537 million gonococci per c.c. The control was the same emulsion heated at 80° for one hour.



Photograph from a cast in Ward VA Royal Infirmary, showing above, a marked positive cutaneous test with a central wheal and surrounding red areola, & below a negative cutaneous test consisting of a small red area at site of injection. Taken twelve hours after intradermal injections were made.

READINGS:- + = Positive
- = Negative
/ = Test not carried out.

TOXIN

TABLE NO. I.

TEST:- .1 Toxin) unheated.
TEST:-.01 Toxin)

CUT.	WASS.	GONOCOC COL C.F.T.	CLINICAL NOTES	BACTERIOLOGY
T —	///	Trace of fixation		
T —			Orchitis recently. Roseolar rash. No proof of G.C..	Gonococci —
T?+	?—	Moderately strong+	G.C. 26 years ago. Epididymitis. Had 2 F vaccine R-V-	" —
T///	—	///		
T —	—		G.C. 3 years ago. Rt.Cowper's abscess burst. P.R.L-V-	" //
T?-				
T?-	///	-	Gumma of hand.	" —
T +				
T?—	—	-	N.P.V.D. Had prostatic abscess and treatment with vaccines. Improving slowly.	" //
T?—				
T?-	-	-	N.P.V.D. Had prostatic abscess and treatment with vaccines. Improving slowly.	" //
T +				
T —	///	-	Old standing syphilis. No proof of G.C.	" —
T//				
T —	-	/	G.C. 3 years ago. Returned now with subacute prostatitis.	" //before - now
T +				
T —	///	/	N.P.V.D. Marked florid secondary.	" —
T?-				
T —	-	/	Extremely bad arthritis. Had arthigon. Improving very slowly.	" //

READINGS:- + = Positive
- = Negative
/ = Test not carried out.

TOXIN

TABLE NO. II.

CONTROL:- .001 Toxin boiled for 10 mins.
TEST:- .001 Toxin.

CUT.	WASS.	GONOCOCCAL C.F.T.	CLINICAL NOTES.	BACTERIOLOGY.	
T – C –	–	Some fix. two doses.	G.C. 10 years ago. Now no trace of V.D.	Gonococci	–
T?+ T –	/	weak +	Attending for 10 weeks. N.P.V.D. Still having F vaccine and still G.C. //	"	//
C – T ±	–	weak + o	G.C. 5 years ago. Treated with medicine only. Now mixed infection.	"	–
C – T –	–	weak +	G.C. 30 years ago. Now bad stricture.	"	– now
C? – T +	///	? + weak	G.C. 9 years ago. Now under treatment for fresh return of Syphilis.	"	–
C – T –	///	Trace of fix. 4 doses.	G.C. 20 years ago. Now under treatment for old syphilis.	"	–
C – T –	–	/// o	G.C. 16 years ago. Within 3 mths. has had F, D and autog. vaccine. - now improving. Has ? G.C. arthritis.	"	– now
C – T –	–	–	N.P.V.D. Marked mixed infection. Getting D vaccine.	"	–
C – T –	–	–	N.P.V.D. Marked mixed infection. No vaccine.	"	–
C – T +	weak +	–	G.C. 19 years ago. Medicine only at that time. Prostate ?	"	–
C + T –	–	–	N.P.V.D. ? Mental.	"	–
C – T +	?–	–	G.C. 8, 4 and 2 years ago. Flat feet. Bursitis of left knee. Had D vaccine and autogenous of mixed organisms.	"	–
C +	–	/	Syphilis 4 years ago. Chancre with Sp. Pallida +	"	–

READINGS:- + = Positive
− = Negative
/ = Test not carried out.

TOXIN

TABLE NO. II. Contd.

CONTROL:- .001 Toxin boiled for 10 mins.
TEST:- .001 Toxin.
(contd).

CUT.	WASS.	C.F.T.	CLINICAL NOTES	BACTERIOLOGY.
F − C −	##	−	Marked Congenital Syphilis.	Gonococci −
F − C −	?−	/	N.P.V.D. Had F (4 doses). Vesicles ?	" −now
F − C −	−	/	N.P.V.D. Prostatic abscess with joint affection. Made good recovery with F vaccine.	" −now

62.

READINGS:- + = Positive
− = Negative
/ = Test not carried out.

TOXIN

TABLE NO. III.

CONTROL:- .0001 Toxin boiled for 10 mins.
TEST:- .0001 Toxin.

CUT.	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY.
T ?− C −	?	weak +	G.C. 3 years ago. Treated in Navy with vaccine.	Gonococci −
T ± C +	##	Moderately strong +	N.P.V.D. Recent fresh attack of G.C. Made good recovery with vaccine.	" ##
T + C ?−	−	weak +	N.P.V.D. Neurasthenic.	" −
T + C −	−	weak +	? G.C. 34 years ago.	" −
T − C −	−	? +	N.P.V.D. Now mixed infection. Had (5) D recently.	" −
T − C ?−	−	? Trace	N.P.V.D. Urethritis for 4 days. Good recovery.	" ##
T + C −	−	? weak pos.	N.P.V.D. Very marked recovery with vaccines (5) F from recent urethritis.	" ## now
T − C ?+	−	Trace of fixation	N.P.V.D. Urethritis for 10 days.	" ##
T − C −	−	weak +	Treated for over 1 year. G.C. ## at first. Now mixed orge. ###	" −
T − C −	−	weak +	G.C. 12, 7 and 2 years ago. Has sore heels and rheumatism in knees.	" −
T − C −	−	−	G.C. 8, 4 and 2 years ago. Mentioned in previous table.	" −
T − C −	−	−	G.C. 20 years ago. Varicocele. Mixed infection. ##	" −
T − C −	−	−	N.P.V.D. Mixed infection. ##	" −
T − C −	−	−	G.C. 8 years ago. Recent urethritis for 14 days. No vaccine.	" ##

READINGS: + = Positive
- = Negative.
/ = Test not carried out.

TOXIN

TABLE NO. III. Cont.

CONTROL:- .0001 boiled for 20 mins.
TEST:- .0001 Toxin.

CUT.	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY.
T - C -	-	Strong +	G.C. 1 year ago. Now has mixed infection - obscure case.	Gonococci — now
T + C?-	-	Moderately strong +	N.P.V.D. Very bad vesiculitis and prostatitis. Cleared up in 9 months.	" ++
T - C -	-	Weak +	G.C. 7 years ago. Fresh attack. Made good recovery with vaccine.	" ?+
T - C -	-	-	Fresh sharp attack of G.C. Ceased attending.	" +-
T - C?+	-	-	N.P.V.D. Clinically nil.	" --
T - C -	-	-	Masturbation. N.P.V.D.	" --
T - C -	-	-	Clinically nil. N.P.V.D.	" —
T?+ C -	-	-	N.P.V.D. Had arthritis as complication of G.C. and attended for 18 months before cured.	" +
T?+ C?+	-	-	G.C. 6 years ago. Rheumatism in knees. Mixed organisms ++	" —
T?- C?-	-	-	Prostatic abscess. Had 2 doses (F) vaccine.	" ++
T - C -	-	/	Has urethritis and arthritis. Responding well to treatment.	" +
T - C -	-	/	Prostatic abscess and epididymitis. Made moderately good recovery.	" ++
T - C -	++	/	Urethritis with G.C. 1 month ago. No treatment. No clinical G.C. now.	" —
T - C -	—	/	Marked G.C.	" ++

READINGS:- + = Positive
− = Negative
/ = Test not carried out.

TOXIN

TABLE NO. III. Cont.

CONTROL:- .0001 Toxin boiled for 10 mins.
TEST:- .0001 Toxin.
(contd).

CUT.	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY.
T − C −	−	−	Seborrhoea. N.P.V.D.	Gonococci −
T − C?−	−	−	Just finished treatment for G.C. urethritis.	" − now
T + C −	weak +	/	Leg ulcer. Not aware of any infection. Has syphilis.	" −
T + C?−	++	/	G.C. 29 years ago. Bad stricture.	" −
T − C −	++	/	Tabes. No history of G.C.	" −
T + C −	−	/	G.C. 1 year ago. Having F and autogenous vaccine Making poor recovery.	" − ++
T − C −	++	/	Double aortic and fibrillation. Chancre 41 years ago.	" −
T − C −	++	/	Has syphilis. No history of G.C.	" −
T?− C −	/	/	Primary Sore. N.P.V.D.	" −
T − C −	/	/	G.C. 2 years ago. Had F vaccine until 3 mths. ago. Good recovery.	" −
T?− C?−	++	/	G.C. 3 times between 20 and 35 years ago.	" −

READINGS:- + = Positive
− = Negative
/ = Test not carried out.

TOXIN

TABLE NO. IV.

CONTROL:- .000001 Toxin heated for 10 mins. at 80° C.
TEST:- .000001 Toxin unheated.

CUT.	WASS.	C.F.T.	CLINICAL NOTES	BACTERIOLOGY
T + C ?−	−	##	G.C. ## "G" 13 years ago. I.P. 7 days. Syph. 1915 P.R. R+ V± . L+ V+ Recovered well.	Gonococci −
T − C +	/	weak +	N.P.V.D. P.R. − G.C. ## Discontinued vaccine.	" +
T ?+ C ?+	−	Moderately strong +	Has had 7 doses F vaccine. Fourth infection. Treated for 2 mths. Now G.C. + Ultimately recovered well.	" +
T ?+ C ?+	−	weak +	No coitus. Simple urethritis − alcohol.	" −
T +pigmented C +	−	+	"G" 6 mths. ago and 5 years ago. Been treated and now G.C. − and considered ready for discharge.	" − now
T − C −	−	##	Never had G.C. at any time. Bad urticaria. Staph. + No treatment required here.	" −
T ± C −	−	?+	G.C. 1½ years ago. No vaccine. P.R. now R+V− L+V−	" −
T + C −	−	weak +	Had Syphilis 2 years ago. Has had 6 F vaccine and reacted very well to treatment.	" +
T + C −	−	weak +	G.C. 4 mths. ago. Had P.R. + Been massaged and had 4 F vaccine. G.C.− now. Doing well with treatment.	" − now
T ± C −	−	##	Pros. abscess. No treatment. G.C. ## Has done moderately well with treatment.	" +
T ?+ C ?+	?−	##	4th infection. G.C. ## Had 7 doses F vaccine P.R. ± Ultimately recovered well.	" ±

READINGS:- + = Positive.
- = Negative.
/ = Test not carried out.

TOXIN

TABLE NO. IV. Cont.

CONTROL:- .000001 Toxin heated for 10-mins. at 80°C.
TEST:- .000001 Toxin unheated.
(contd.)

CUT.	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY.
T?+ C?+	-	/	G.C. +++ Developed prostate but ultimately did well.	Gonococci +
T - C?±	+++	/	Old syphilis. No history of G.C.	" —
T - C?-	+++	/	" " " " " "	" —
T - C -	++	/	" " " " " " Case of gumma of both clavicles.	" —
T + C +	—	/	G.C. ++ Had F 3 dozes. Appears to have small resistance.	" +-
T?+ C?+	/	/	G.C. treated here and at Dundee. Stricture. PM.± No vaccines here.	" —now
T + C -	—	/	G.C. 2 years ago treated here. Now fresh attack and has had F vaccine. Ready for discharge.	" —now
T + C?-	—	/	After G.C. ++ and treatment by vaccines and tests for cure, is ready for discharge.	" —now
T?+ C -	—	/	G.C. before ? time. Now has moderate mixed infection urethritis.	" —
T + C +	—	/	G.C. 6 years ago. Had vaccines then. Now has balanitis and non-G.C. urethritis.	" —
T - C -	—	/	P.R. +++ G.C. ++ Been treated for 7 weeks. Very acute case.	" +
T - C -	—	/	Primary sore. Pallida +. No G.C. Never had G.C.	" —

READINGS:- + = Positive.
- = Negative.
/ = Test not carried out.

TOXIN

TABLE NO. IV. Cont.

CONTROL:- .000001 Toxin heated for 10 mins. at 80° C.
TEST:- .000001 Toxin unheated.
(contd.)

CUT.	WASS.	C.F.T.	CLINICAL NOTES	BACTERIOLOGY.
T+ C?-	-	-	Treated previously for G.C. Now bad mixed infection but recovered well.	Gonococci —
T?+ C -	-	-	Syphilis 3 years ago. No previous G.C.	" —
T +/ C -	-	-	G.C. 20 years ago. Now no G.C. and very slight urethritis.	" —
T +/ C +/ C -	-	-	G.C. 1 year ago and now has residual mixed infection in prostate.	" —
T +/ C -	-	-	Had Pros. massage and F.and D vaccines. Much improved.	" —
T +/ C -	-	-	Nothing found.	" —
T - C?-	-	-	Very marked mixed infection.	" —
T - C -	-	-	Everything absolutely minus.	" —
T - C +/	-	-	Mixed infection +/+ and has done well with D vaccine.	" —
T +/ C?-	-	-	N.P.V.D. G.C.-. Slight mixed infection and did well with D vaccine.	" —
T?+ C?-	-	-	G.C. twice previously. Had 3 doses D vaccine previously.	" —
T + C -	+/	-	Case of syphilis under treatment. No G.C. now or previously.	" —
T - C?-	-	/	N.P.V.D. G.C.-+/+ Developed prostatitis but ultimately did well.	" —

READINGS: -/- = Positive
- = Negative
/ = Test not carried out.

TOXIN

TABLE NO. IV. Cont.

CONTROL:- .000001 Toxin heated for 10 mins. at 80°C.
TEST:- .000001 Toxin unheated.
(contd.)

CUT	WASS.	C.F.T.	CLINICAL NOTES	BACTERIOLOGY.
T - C -	-	Weak -/-	N.P.V.D. Had pros. and epididymis and 10 doses F vaccine. Ultimate recovery good.	Gonococci -/-
T -/- C + -	-	Strong -/-	Syphilis 7 years ago. G.C. 13 years ago. Fresh attack G.C. -//- P.R. R-V- L±V+ Recovered well.	" -/-
T - C ?-	-	Weak -/-	N.P.V.D. G.C.-//- ant. urethritis only.	" -/-
T -- C -	-	-	Recurrence of soft sore and mixed infection. Vaccine 3 years ago. No G.C.	" —
T - C -	-	-	G.C. /// fresh urethritis. N.P.V.D. No vaccine.	" -/-
T -/- C -	-	-	Fresh attack. Only ant. urethritis. G.C.-//, but did very badly with treatment.	" -/-
T - C -/-	? -	?-	G.C. 20 years and 8 years ago. Pros. abscess. Had 7 F and 2 D vaccines.	" -/-
T ± C -	-	-	R+V+ P.R. L+V+. N.P.V.D. G.C. -//- Treatment results bad.	" -/-
T - C -	-	-	Had G.C. 2 years ago. Has been treated for 8 months with F and D vaccine, etc. Now for discharge. Responded well to treatment.	" -/-
T + C ± -	-	-	Ant. and Post. urethritis of 3½ weeks duration. No treatment. Had F 2500 coincidently.	" -/-
T + C - +	-	? trace.	R + V- G.C. 4 years ago. Fresh attack. G.C. P.R. L-//V- . Did well with treatment.	" -/- -

READINGS:- + = Positive
− = Negative
/ = Test not carried out

TOXIN

TABLE NO. IV.Cont.

CONTROL:- .000001 Toxin heated for 10 mins. at 80° C.
TEST:- .000001 Toxin unheated.
(contd).

CUT.	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY.
T ?+	?	−	G.C. 1 year ago and again now. Did well with treatment.	Gonococci /
C ?+				
T +	−	−	Venerophobe. Everything negative.	" −
C −				
T ±	−	−	G.C. 1 year ago. G.C. /// Had 300 mill. prov. poly. vaccine the day before.	"
C ±				" /
T ±	−	−	No G.C. Diph. ///. Very slight case of mixed infection.	" −
C −				
T +	−	−	3 mths. ago had 4 mths. of vaccine. At first G.C. ///. Had had all tests of cure and discharged.	"
C ?−				" − now
T ?+	−	−	Mild urethritis. G.C. always −. Discharged shortly.	" −
C ?+				
T ?+	−	−	Never had G.C. Had prov. inj. 3 days before.	" −
C ?+				
T −	−	−	G.C. 4 years ago. Recent mixed infection. No G.C. now.	" −
C ?−				
T −	−	−	Not aware of infection. Everything negative.	" −
C −				
T −	−	−	Very slight non-G.C. urethritis. G.C.−. N.P.V.D.	" −
C ?+				
T −	−	−	Never anything positive found.	" −
C −				
T −	−	−	Non-G.C. urthritis.	" −
C ?−				
T −	−	? −	G.C. in India 3 years ago. Recent G.C. ///. Reacted very well to treatment.	" −
C ?−				" −
T −	−	−	5 years ago. Had D vaccine. G.C. never found.	
C −				

READINGS:- + = Positive
− = Negative
/ = Test not carried out.

TOXIN

TABLE NO. IV. Cont.

CONTROL:- .000001 Toxin heated for 10 mins. at 80°C.
TEST:- .000001 Toxin unheated.
(contd).

CUT.	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY.
T − C −	−	/	Fresh case. G.C. ## Had initial vaccine 3 days ago. Responded well to treatment.	Gonococci +
T + C +	−	/	G.C. 15 years ago. Now fresh attack. G.C. # Results of treatment bad.	" +
T?+ C −	−	/	G.C. # Epididymitis - slow recovery. Ultimately quite good.	" +
T − C?+	−	/	G.C. ## No vaccine. Results of treatment very good.	" +
T − C −	−	/	Diphtheroids /##. G.C.-. Never had G.C. D.Gs, all neg.	" −
T − C −	−	/	G.C. ## very bad case with slow recovery. Long incubation period.	" +
T + C +	−	/	N.P.V.D. G.C. # Result of treatment good.	" +
T − C −	−	/	Case now undergoing tests of cure and G.C. now neg. Was bad case at first.	" − now
T + C +	///	/	Syphilis 19 years ago. Now has fresh acute G.C.	" ##
T + C −	−	/	N.P.V.D. G.C. ## Extremely good result from administration of F vaccine.	" ##
T?− C?−	−	/	N.P.V.D. G.C. ## Clinically slight, but reacted slowly to treatment.	" ##
T + C −	−	/	N.P.V.D. G.C. # Uncomplicated and reacted very well to treatment.	" ##

READINGS:- + = Positive
− = Negative
/ = Test not carried out.

TOXIN

TABLE NO. IV. Cont.

CONTROL:- .000001 Toxin heated for 10 mins. at 80°C.
TEST:- .000001 Toxin unheated.
(contd).

CUT.	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY
T + C +	−	/	Never had G.C. Sore non-specific. Ready for discharge.	Gonococci −
T ?+ C −	−	/	G.C. // P.R. /// Responded to treatment and F vaccine.	" //
T − C ?+	/	/	I.P. 21 days. Alcohol //. Doing badly.	" −
T ?− C ?−	−		No V.D. of any kind.	" −
T − C −	−	/	No V.D. of any kind.	" −
T − C −	/	/	Ant. urethritis G.C. // Did well with treatment.	" //
T − C +	/	/	L.P. 27 days. P.R. //. Very acute case but did well with treatment.	" //
T + C +	/	/	Very acute first attack. G.C. // Did very badly.	" //
T + C −	/	/	Mixed infection. /// G.C. never found.	" −
T ?+ C +	/	/	G.C. 10 years ago and had recurring "gleet" since.	" −
T − C −	/	/	Sore 3 years ago. Clinically absolutely negative.	" −

READINGS:- + = Positive
- = Negative
/ = Not carried out.

DETOXICATED VACCINE.

TABLE NO. V.

Toxin results given for comparison.

Test:- 0·1c.c. containing 2,500 millions gonococci

CUT.	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY
++	-	Moderately strong +	Toxin 1/10 also ++ G.C. 8 years before. Now prostatic abscess. Recovery poor.	Gonococci ?-
+	-	/	" " " ? + Under treatment. Having vaccines. Responding well.	" +
+	-	/	" " " + Very poor result. Has arthritis. Had F and arthigon. G.C. 3 years ago. Still bad.	" +
++	-	/	" " " ± Prostatic abscess with epididymitis. Good recovery.	" +
—	-	/	Toxin nil. Prostatic abscess.	" +
++	-	/	Toxin nil. Had vaccines. Responding to treatment (T.B.) Post Urethritis. Arthritis.	" +
—	-	/	Toxin + Not responding to treatment.	E.C. +
+	-	Weak +	Toxin + Chronic infection and mixed organisms. No T.B. found.	E.C. —
—	-	-	(Toxin ± Had 2 doses of vaccine. Epididymitis) Prostatic abscess.	E.C. ++
—	-	/	Toxin nil. Prostatic abscess and epididymitis. Made moderately good recovery.	E.C. ++
+	-++	/	Toxin nil. Arthritis. No treatment. No clinical gonorrhoea.	E.C. —
—	-	/	Toxin nil. Acute E.C. urethritis. Good recovery.	E.C. +++

READINGS:- + = Positive.
- = Negative.
/ = Test not carried out

T = Test.
C = Control.

LIPOID FRACTION.

TABLE NO. VI.

TEST:- .00001 c.c. Lipoid Fraction.
CONTROL:- .5% Carbol Saline.

CUT	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY
T + + + C ? + -	-	Weak +	G.C. 11 years ago. Now ? nil.	Gonococci.
T - C -	-	?-	Recurrent iritis. No venereal history. Iritis improved with treatment.	" -
T - C -	-	-	G.C. 3 years ago. Had vaccines. Now mixed organisms ###	" -
T - C -	-	-	G.C. 1 year ago. Good recovery.	" -
T - C +	##	-	? V.D. 10 years ago. Now has syphilis. No G.C.	" -
T + + C +	/	-	G.C. twice previously. Now fresh attack. Good recovery.	" +
T + + C +	-	-	Chronic coitus and debauchery. Prostatic abscess. Good recovery.	" ###
T - C -	-	-	G.C. 8 years ago. Nil now. Diabetes.	" -
T - C -	-	-	G.C. about 8 times. F2500 1 week ago. Mixed organisms ###	" -
T - C -	-	-	N.P:V.D. Mixed organisms ###	" -
T - C -	-	-	G.C. 3 times previously. Had F 2500. Has ? fresh attack.	" -
T - C +	/	/	No V.D.	" -
T - C ? -	-	/	G.C. 8 years ago. Now fresh attack. Tendency to papule formation.	" ##

With Lipoid Fraction there is a distinct tendency to papule formation instead of the usual erythema or wheal.

READINGS:- + = Positive
- = Negative
/ = Test not carried out

GONOCOCCAL PROTEOSE.

TABLE NO. VII.

TEST:- .0001 c.c.) both on the same forearm.
TEST:- .001 c.c.)

CUT.	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY.
+	/	weak +	Treated for G.C. for 5 months. Ready for discharge. Had last F vaccine 5 months ago.	Gonococci - now
+	-	///	Infected one year ago, and reinfected since. Becoming worse in spite of treatment.	" //
±	-	weak +	G.C. 2 years ago. Treated here, now free from infection (Gave persistent + with .000001 toxin - heated toxin control negative.	" // before - now
+	-	Moderately strong +	G.C. 2 years ago. Now mixed organisms. Did well with treatment	" -
+	///	weak +	G.C. 1 year ago. Has arthritis. Mixed organisms.	" -
+	?-	weak +	G.C. for 3 - 5 mths. Now being discharged. Has had vaccine.	" -
+	-	- o	N.P.V.D. Hypospadias. No V.D.	" -
+	-	- o	" No V.D. present.	" -
?+	-	?+	G.C. 5 years ago. Fresh attack - getting vaccine. Doing badly.	" -
+	-	-	G.C. 3 years ago. Ready for discharge. Provocative polyvalent 3 weeks ago.	" -
±	-	-?	G.C. 1 year ago. Fresh attack. Has had no vaccine but responded to it well later.	" //

READINGS:- + = Positive
- = Negative
/ = Test not carried out

GONOCOCCAL PROTEOSE.

TABLE NO. VII. Cont.

TEST:- .0001 c,c.
TEST:- .0001 c.c.
(contd.)

CUT.	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY.
±	+	-	N.P.V.D. No G.C. present.	Gonococci -
±	-	-	G.C. 2 years ago. Now mixed infection.	" -
?+	-	-	G.C. 20 years ago. Has had (F and D) vaccine for 3 mths. Ready for discharge.	" -
-	-	-	No V.D. of any kind.	" -
+	-	-	G.C. 14 mths. ago. Now ready for discharge.	" -
?-	-	/	Never G.C.	" -
+	-	/	G.C. 8 years ago. Now has syphilis.	" -
+	-	/	N.P.V.D. All findings negative.	" -
?+	/	/	G.C. 6 years ago. Now fresh attack - fairly severe.	" ##
-	##	/	?G.C. 25 years ago. Old syphilis. Fresh attack - has lasted 11 days.	" ##
+	/	/	N.P.V.D. Has had an apparently mild attack. Poor recovery.	" ##

READINGS:- + = Positive
− = Negative
/ = Test not carried out

.00001 PROTEOSE.

TABLE NO. VIII.

CUT.	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY.
−	?−	weak +o	Locomotor. — Had prov.. polyvalent vaccine and G.C. neg. in all smears. ? Urethritis. R + V —	Gonococci −
+ Papule	−	Moderately strong +	Has gleet. G.C. 2 years ago. Now L − V − No smears.	" −
−	−	strong +o	G.C. 18 and 10 years ago. Now has fresh G.C. with P.R. + + and G.C. // and epididymitis.	" //
±	−	− o	?V.D. infection 20 years ago. Now has pityriasis rubra (and or) seborrhoea.	" −
+	//	/ o	? G.C. 16 years ago. No evidences now of infection or remains	" −
±	//	/	Syph. 30 years ago. Now ulcus couris. ?? G.C. 30 years ago.	" −
−	/	/	Stricture. G.C. 14 years ago. Now G.C. − and no "active" focus.	" −
−	/	/ o	Epididymitis — had F 5000 I.P. 4 weeks.	" +
−	/	/ o	Prostatic abscess. Had F 2500 and F 5000. Apparently very small resistance.	" +
+	/	/	Vaccine with test. G.C. // N.P.V.D. Did well with treatment.	" +
−	/	/	−? Infection 2 years ago. Fresh recurrence with P.M. + and Epididymitis.	" +

READINGS:- + = Positive.
- = Negative.
/ = Test not carried out.

-.00001 PROTEOSE

No control

TABLE NO. VIII. Cont.

CUT.	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY.
±	-	Weak +	Never had G.C. or any V.D. Nil found.	Gonococci —
-	-	?? ±	G.C.+ 2 months ago. Full course F vaccine. Now for discharge. Good recovery.	" -/-
-/-	-	Weak +	G.C. //- P.R.+. Had full course F vaccine. Progress moderate.	" -/-
-	-	Weak +	G.C. //-. Been attending for 5 months and recovered from epididymitis with F.D. and autog. vaccine. Not good recovery.	" --/
+ —	-	Weak +	Syphilis twice. G.C. 6 times. Made good recovery.	" -now
+ -	?	Weak +	G.C. P.R. -//-. Had F vaccine. Recovery slow but complete.	" -//-
-/-	-	-//	G.C. 4 months ago neglected. Recurrence after coitus. Bad progress.	" -/-
-/-	-	-// to -///	Post. urethritis. P.R.+ . Had full course F vaccine. Recently cleared up.	" -now
-	-	±	G.C. -//- . Prostatic abscess. Had 3 F vaccine just before.	" -//-
+ -	?	-//	N.P.V.D. Nothing except phymosis.	" -
+	?	-//	G.C. 7 years ago. Again G.C. with P.R. R+ L+ Had 4 F vaccine.	" -//

READINGS:- + = Positive.
- = Negative.
/ = Test not carried out.

.00001 PROTEOSE. (contd).

TABLE NO. VIII. Cont.

CUT.	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY.
+	/	/	Acute G.C. I.P. 8 days. P.M. - G.C. ~~+++~~. Developed post. urethritis in spite of treatment and F vaccine.	Gonococci ~~+++~~
-	-	/	Primary syphilis. N.P.V.D. No G.C.	" -

READINGS:- + = Positive.
- = Negative.
/ = Test not carried out.

PROTEOSE.

TABLE NO. IX.

CONTROL:- .5% Carbol Saline
TEST:- .000001 c.c.

CUT.	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY.
	?	Weak	Has had F vaccine for 3 months. Now ready for discharge.	Gonococci -
	-	-	11 years ago had ? V.D.	" -
-	-	-	G.C. 3 years ago in Russia. Nil now. Did well with D vaccine.	"- -
	-	-	G.C. 35 years ago. Stricture and cystitis now.	" -
papule.	-	-	Very marked mixed infection. No sign of G.C.	" -
-	-	-	Nil.	" -
-	-	-	G.C. 6 years ago. No G.C. now.	" -
	-	-	N.P.V.D. non-gonococcal urethritis.	" -
papule	-	-	G.C. Done moderately with treatment.	" ++-
erythema	-	/	G.C. 2 years ago. Treated here. Had full treatment including provocative.	" -+
	/	/	Post. urethritis - doing badly.	" ++
papule	-	/	G.C. 4 years ago in France. Now has primary chancre.	" -
++	/	/	Recent bad G.C. Has done badly with treatment.	" +++
-	/	/	" " G.C. " " well " "	" +-

READINGS:- + = Positive
− = Negative
/ = Test not carried out.

.000001 PROTEOSE.

TABLE NO. IX. Cont.

CUT.	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY.
±	−	−	Never had G.C. Case of treated syphilis. Died of hemiplegia.	Gonococci −
//	−	−	Recent fresh G.C. Made a good recovery with F vaccine.	" /
/	−	−	G.C. ?3 years ago. Now non-G.C. - Urethritis.	" −
/	−	−	G.C. + Having F vaccine. P.R.? Made good recovery.	" /
/	−	−	? Congenital specific. No G.C.	" −
±	?−	−	Post. urethritis. G.C. // Ceased attending.	" /
−	//	−	No G.C. now. ?G.C. 16 years ago. Under treatment for syphilis. R + V −	" −
−	−	−	? Mixed infection P.R. L + V − Never had found G.C.	" −
±	−	−	N.P.V.D. Non-G.C. recent urethritis. No complications. Has had F 2500.	" −
±	−	−	N.P.V.D. Non-G.C. recent urethritis. No complications. Has had F and D 2 doses.	" −
±	−	−	N.P.V.D. G.C. //. Later got prostate and epididymis. Not good recovery.	" //
−	?	−	Reporting with epididymitis as result of G.C. neglected. Ultimately did well.	" //

READINGS:- + = Positive
− = Negative
/ = Test not carried out

.000001 PROTEOSE.

(contd).

TABLE NO. IX. cont.

CUT.	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY.
+	?	?±	Reporting with mixed infection. Ceased attending. G.C. not found.	Gonococci −
−	−	−	G.C. (1) H (2) H.. Had F vaccine 5000 coincidently. Recovered well.	" /
?−	−	−	Gonophobia.	" −
−	?−	?−	? 15 years ago. Has stricture and non-G.C. urethritis.	" −
weak +	−	?−	No history of G.C. Mixed infection urethritis. Cleared up quickly.	" −
+	−	−	Chancre 20 years ago and ? G.C. 14 years ago. Nothing now. No treatment.	" −
strong +	−	−	Just developed epididymis from G.C. urethritis. Did badly.	" +
−	−	weak +	Never had G.C. Mercurial stomatitis and syphilis under treatment.	" −
+	−	strong +	G.C. P.R. +. Epididymis. Had 6 F vaccines.	" /
±	//	weak +	G.C. about 10 years ago. Stricture. No vaccine. Has had G.C. more than once.	" − now

READINGS:- + = Positive
− = Negative
/ = Test not carried out

.000001 PROTEOSE.

TABLE NO. IX. Cont.

CUT.	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY.
+ fading	−	−	Case of Ord. G.C. Done well with treatment and is discharged cured.	Gonococci − now
−+	−	−	Case of G.C. // which has just had F vaccine and discharged after 4 months treatment.	" − now
/	−	+ −	Post. urethritis with G.C. // and with pros. and vesicles. Evidently very poor resistance. Stopped attending.	" /
/	−	−	G.C. 35 years ago. Now has stricutre with cystitis mixed infection. Autog. vaccine.	" −
/	−	−	Case of masturbation. No V.D. whatever.	" −

READINGS:- + = Positive
- = Negative
/ = Test not carried out.

PROTEOSE

TABLE NO. IX. Cont.

CONTROL:- 5% Carbol Saline.
TEST:- .000001 c.c.
(contd).

CUT.	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY.
+ Erythema	/	/	G.C. 37 years ago. Now has small stricture.	Gonococci -
+ Erythema	/	/	G.C. 4 years ago. A fresh attack.	" +
-+	-	/	Syphilis. Ready for discharge. No G.C.	" -
+ Erythema	-	/	? G.C. 6 years ago. Nothing now.	" -
+	+	/	Had D. and F vaccine and ready for discharge.	" -
-	/	/	G.C. 50 years ago. Marked stricture.	" -
+ Papule	++	/	Congenital syphilis.	" -
+	/	/	G.C. 29 years ago. Now stricture.	" -
+ Erythema	-	/	G.C. 11 years ago. Treated for 3 mths. for fresh attack. Had F vaccine.	" +

READINGS:- + = Positive.
- = Negative.
/ = Test not carried out.

PROTEOSE.

CONTROL:- .5% Carbol Saline.
TEST:- .0000001 c.c.

TABLE NO. IX. Cont.

CUT.	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY.
T C -	-	Weak	Had recent attack with prostatic involvement and F vaccine.	Gonococci ++
T C -	?-	-	G.C. 2 years ago. Recently had 300 mill. prov. vaccine.	" -
T C -	-	?Trace	G.C. 30 years ago. Nil now.	" -
T C -	++	Weak	Syphilis 33 years ago. G.C. 3 times. Rheumatism and Iritis.	" -
T C -	-	-	N.P.V.D. Never aware of any infection.	" -
T C -	-	-	G.C. 5 years ago. Nothing since.	" -
T C -	-	-	Making very bad recovery from recent G.C.	" ++
T?- C -	-	-	Balanitis. No V.D.	" -
T C -	-	-	G.C. treated here. Left before treatment completed.	" -+
T C -	-	-	G.C. 2 years ago. Has arthritis.	" -
T?- C?-	/	-	Fresh G.C. 5 days ago. Made good recovery.	" +
T C -	/	-	No V.D. of any kind.	" -
T C -	-	-	Just finished 3 months treatment for G.C. including F vaccine. Good result. Now ready for discharge.	" -no

READINGS:- + = Positive.
- = Negative.
/ = Test not carried out.

PROTEOSE.

TABLE NO. IX. Cont.

CONTROL:- .5% Carbol Saline.
TEST:- .0000001 c.c.
(contd.)

CUT.	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY.
T ++ C -	-	?	Both G.C. and Syph. previously. Been treated for 6 mths. for mixed infection with D vaccine.	Gonococci -
T - C -	-	-	Had G.C. with prostatic abscess and much treatment. Now ready for discharge.	" -
T - C -	-	-	Had prostatic abscess. No G.C. found.	" -
T - C -	-	-	Treated here 1 year ago for G.C. Now nil.	" -
T - C -	-	-	N.P.V.D. Nil.	" -
T - C -	-	-	? G.C. 1 year ago. Now has muscular pains and small joint arthritis.	" -
T - C -	-	-	Instrumentation 5 years ago. No symptoms. Desires test of cure.	" -
T - C -	/	-	Old G.C. Had F2500 1 week before.	" -
T C -	/	-	No evidence of V.D.	" -
T? C -	-	-	G.C. twice in last 5 years. Now nil.	" -
T - C -	-	-	Venerophobe. All findings negative.	" -
T C -	-	-	Been treated for 6 months for G.C. Had prostate and arthritis.	" ++
T - C -	-	-	G.C. 3 years ago. Now nil.	" -

READINGS:- + = Positive
– = Negative
/ = Test not carried out

PROTEOSE.

TABLE NO. IX. Cont.

CONTROL:- .5% Carbol Saline.
TEST:- .0000001 c.c.
(contd).

CUT.	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY.
T + C –	–	–	Never had any V.D. Balano-posthitis.	Gonococci –
T // C ?+	–	–	G.C. 10 years ago. Recent treatment for syphilis. Has had dermatitis and jaundice from arsenic.	" –
T + C –	–	–	Mixed infection. Never had G.C.	" –
T – C –	–	//	G.C. 7 years ago. Given provocative - gonococcal vaccine just before.	" –
T ?– C –	//	//	G.C. 1½ years ago. Discharged cured. No G.C. now.	" –
T – C –	–	+	N.P.V.D. Subacute arthritis. Bad teeth. No evidence of G.C.	" –
T – C –	//	–	G.C. 7 years ago. No evidence now.	" –
T – C –	–	–	G.C. 3 mths. ago. Treated then with F vaccine. Now ready for discharge.	" –
T // C –	–	–	G.C. 8 years ago. Now rheumatism in small joints of feet.	" –
T // C –	–	–	G.C. 5 years ago. Given prov. just before.	" –
T – C –	–	–	N.P.V.D. Everything negative.	" –
T – C –	–	–	N.P.V.D. (?) Dermatitis - left hand.	" –
T – C –	–	–	N.P.V.D. All negative.	" –

READINGS:- + = Positive
− = Negative
/ = Test not carried out

PROTEOSE.

CONTROL:- .5% Carbol Saline.
TEST:- .0000001 c.c.
(contd).

TABLE NO. IX. Cont.

CUT..	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY.
T −	−	−	G.C.. 1 year ago. Now nil.	Gonococci −
C −				
T −	−	−	Nil.	" −
C −				
T +	−	/	Infected with G.C. 16 days ago. Now has urethritis.	" ++
C −				
T −	−	/	Very bad reinfection after G.C. 4 years ago. Made good recovery.	" ++
C −				
T +	−	/	G.C. 13 and 10 years ago. Has syphilis.	" −
C −				
T +	/	/	Treated on and off for 18 months. Had F vaccine. Now ready for discharge.	" −
C ±				
T −	−	/	N.P.V.D. Completed treatment for Syphilis. Discharged cured.	" −
C −				
T −	/	/	G C 1½ years ago. Recently had 2 F vaccine.	" −
C ±				
T −	/	/	Acute G.C. contracted 21 days ago.	" ++
C −				

READINGS:- + = Positive
– = Negative
/ = Test not carried out.

PROTEOSE.

TABLE NO. X.

CONTROL:- .0005 Proteose boiled for 10 minutes.
TEST:- .0005 Proteose.

CUT.	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY.
T +	/	strong +	Treated for G.C. 18 mths. ago. Now states was discharged from Cardiff 6 months ago.	Gonococci –
C ?+				
T +	–	weak +	G.C. 3 times in last 10 years. Now has rheumatism and sore heels.	" –
C –				
T ?±	–	weak +	2 mths. ago had G.C. ## Treated and had 6 F vaccine. Made good recovery.	" –
C –				
T +	–	?+	Staphylococcal urethritis. Never any V.D.	" – now
C –				
T +	–	? weak +	Recent G.C. Made marvellously quick recovery with F vaccine 3 weeks ago.	" – now
C ?–				
T –	–	weak +	G.C. 2 years ago, and 3 mths. ago. Made good recovery with F and D vaccine. Now ready for discharge.	" –
C –				
T ±	–	?±	G.C. 18 mths. ago. Left before cure complete.	" –
C ±				
T ±	–	?±	? G.C. 3 years ago. Clinically nil.	" +
C ±				
T +	##	Moderately strong +	N.P.V.D. Recent G.C. Doing well with treatment.	" +
C ?–				
T +	–	weak +	G.C. and bubo 3 years ago. Doing well with treatment for recent G.C.	" –
C ±				
T –	–	weak +	G.C. 3 years ago. Now fresh subacute attack.	" –
C –				
T –	–	?±	N.P.V.D. Now fresh acute G.C.	" ##
C –				

READINGS:- + = Positive
− = Negative
/ = Test not carried out.

PROTEOSE.

TABLE NO. X. Cont.

CONTROL:- .0005 Proteose boiled for 10 minutes.
TEST:- .0005 Proteose.

CUT.	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY.
T − C −	−	−	No sign of V.D.	Gonococci −
T ± C ±	−	−	G.C. 1 year ago. Now nil.	" −
T − C −	−	−	Venereal warts before. Now slight mixed infection.	" −
T + C +	−	?−	Just recovered from G.C. and had F vaccine.	" ++
T − C ±	+++	?−	G.C. 1 year ago. Treated with vaccines. Now has fresh attack.	" ?+
T − C −	−	−	Syphilis and G.C. 5 years ago. Now secondary organisms.	" −
T + C −	−	−	Syphilis and G.C. 8 years ago. Now warts and a few secondary organisms.	" −
T − C +	−	−	Recent G.C. N.P.V.D. Psoriasis.	" +
T + C ±	−	−	Never had G.C. Alcohol +++ and mixed organisms.	" −
T ± C ±	−	−	N.P.V.D. Recent fresh urethritis, slow but good recovery.	" +
T − C −	−	/	Syphilis and G.C. 6 years ago.	" −
T + C ±	/	/	N.P.V.D. Now well marked fresh G.C.	" +

READINGS:- + = Positive
− = Negative
/ = Test not carried out.

PROTEOSE.

TABLE NO. X. Cont.

CONTROL:- .0005 Proteose boiled for 10 minutes.
TEST:- .0005 Proteose.
(contd.)

CUT.	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY.
T − C −	−	Moderately strong +	G.C. 2½ years ago. Recent fresh attack. Made good recovery.	Gonococci −
T + C ±	−	weak +	G.C. 18 mths. ago. Treated here. Now mixed organisms. Otherwise nil.	" −
T ± C ±	−	Moderately strong +	Had recent G.C. for 21 days. Otherwise nil.	" #
T − C −	/	−	G.C. over 1 year ago. Discontinued treatment. Now has arthritis.	" −
T − C −	−	−	N.P.V.D. Neurasthenic.	" −
T + C +	−	−	G.C. 13 years and 1 year ago. Treated with F and D vaccine. Bad arthritis. Poor recovery.	" − now
T + C −	−	−	G.C. 1 year ago. Nothing now.	" −
T − C −	−	−	No signs of G.C. Slight mixed infection.	" −
T ?+ C −	−	−	Diabetes. No sign of V.D.	" −
T + C ±	−	−	G.C. 8 times! Syphilis 6 years ago. Now has mixed infection.	" −

READINGS:- + = Positive
− = Negative
/ = Test not carried out.

PROTEOSE.

TABLE NO. X. Cont.

CONTROL:- .0005 Proteose boiled for 20 minutes.
TEST:- .0005 Proteose.

CUT.	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY.
T − C −	/	/	G.C. 9 years ago. Now has acute Cowperitis and post. urethritis. Mixed organisms ///.	Gonococci −
T − C −	−	/	G.C. 6 years ago. Now has fibrosed prostate nothing else.	" −
T − C +	−	/	Recently completed treatment for G.C. Had F and D vaccine.	" − now
T ± C +	−	/	Recent G.C. Made fair recovery.	" //
T − C −	/	/	N.P.V.D. A few mixed organisms.	" −
T − C +	/	/	? 2 years ago. Alcohol. //	" −
T − C −	/	/	N.P.V.D. A few mixed organisms.	" −
T − C ±	/	/	G.C. 3 years ago. Recent attack with epididymitis.	" +
T + C −	/	/	Recent G.C. urethritis (ant.) Made good recovery with F vaccine.	" +
T − C −	/	/	N.P.V.D. Simple balanitis.	" −

READINGS:- + = Positive
- = Negative
/ = Test not carried out.

.1 cc. POLYVALENT EMULSION. - 20 strains.

TABLE NO. XI.

CONTROL:- ./c.c. Polyvalent Emulsion - 20 strains - heated at 80°C for 1 hour.

CUT.	WASS.	C.F.T.	CLINICAL NOTES.	BACTERIOLOGY.
T +++ C -	-	strong +	Acute G.C. 7 months ago. Epididymitis. Had 2 courses F vaccine, arthigon and autogenous.	Gonococci ++
T ++ C -	-	? neg.	N.P.V.D. Epididymitis. No vaccine. Good recovery.	" ++
T ++ C -	-	++	G.C. 22 years ago. Periurethral abscess.	" ++
T ± C -	-	++	No active V.D. present. No definite history.	" -
T ++ C -	-	Trace of fixation	G.C. 4 years ago.	" -
T + C -	-	-	N.P.V.D. Had F2500 Post. urethritis with P.R. ++	" ++
T - C -	/	//	Pus tube removed 5 days ago.	No Bacteriology
T - C -	/	/	Retroverted uterus. No evidence of G.C.	Gonococci -
T + C -	/	/	? Arthritis.	? -
T + C -	/	?±	? Arthritis.	? -
T + C -	/	/	? Arthritis.	? -
T ++ C -	/	/	Child 15 days old. G.C. cultures from synovial pus of arthritic joint.	Gonococci +
T ++ C -	++	/	Marked G.S. No G.C.	" -
T - C -	/	/	History of G.C. Cannot be found now. Has mammary abscess.	" -
T + C -	-	/	Recent acute ant. urethritis.	" +

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